

### 3. Non-Technical Abstract

Despite the availability of safe and effective dental caries prevention measures, including daily oral hygiene procedures, community water fluoridation, and professional use of topical fluoride and dental sealants, tooth decay remains a major health problem afflicting a majority of the population in the U.S. and worldwide. The proposed research is intended to develop, and ultimately commercialize, a novel biotechnology called replacement therapy to aid in the prevention of this disease.

A2JM is a naturally occurring *Streptococcus mutans* strain, originally isolated from a human subject, which has been genetically modified. *In vivo* studies showed that the genetic modifications greatly reduced pathogenic potential and increased colonization potential. Laboratory and animal testing indicate that this strain can substantially improve existing preventive measures and result in significant public health benefits with concomitant savings in national health care costs.

To further develop replacement therapy for use in humans, Oragenics, Inc. has designed and standardized a manufacturing process for preparation and storage of A2JM doses and a mouth rinse containing the amino acid, D-alanine. To date, neither A2JM nor D-alanine rinse has been evaluated in humans. Therefore, safety will be evaluated in human subjects under an IND for Phase 1 clinical trials. A rapid, convenient and reproducible test for monitoring implantation of A2JM has also been developed. If the specific aims of the Phase 1 clinical trial are successfully achieved, the result will be a complete and validated system for delivery to the oral cavity and monitoring to insure successful implantation of A2JM in humans. The next step would be to evaluate the long-term safety and the anti-caries effectiveness of A2JM implantation in a large scale Phase 2/3 clinical trial.